Using Nanotechnology to Detect Nerve Agents

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Nanotechnology has opened a wide range of opportunities having potential impacts in areas as diverse as medicine and consumer products. In collaboration with researchers at the University of Toledo (UT), Air Force Institute of Technology (AFIT) scientists are exploring the possibility of using a nanoscale organic matrix to detect organophosphate (OP) nerve agents. Current techniques for detecting OP compounds are expensive and time consuming. Developing a nanoscale organic matrix sensor would allow for direct, real-time sensing under field conditions. This article describes the science behind such a sensor and its possible applications.

High-performance sensors are needed to protect Soldiers and civilians from attack. At present, doctrine requires Air Force units to resume their primary mission within two hours of a chemical or biological strike.[1] Meeting the two-hour operational goal may mean the difference between defeat and victory. However, OP detection capabilities now in place are limited in sensitivity, time required to operate, and ease of use, making the specified two-hour window difficult to meet.

In the event of a chemical attack, military personnel must have the most sensitive and rapid means available of detecting and quantifying the concentrations of chemical agents. For example, VX, one of the most lethal and persistent nerve agents, causes death in 50 percent of the population at a concentration of approximately 1.2 milligrams per cubic meter (mg/m^3) after a 10-minute exposure.[2] This concentration is about the same as one teaspoon of agent released into a one-meter-high layer of air covering the area of a football field. At this concentration, equipment currently in the inventory can easily detect VX. However, after a three-hour exposure, VX at a concentration of about 0.08 mg/m^3 (15 times lower) will still cause death. Unfortunately, these low concentrations are at or below the detection limits of conventional chemical-warfare-agent equipment. Similarly, 50 percent of the population will experience nonlethal yet mission-inhibiting effects such as pinpointing of the pupils and nausea or vomiting at 0.01 mg/m^3 after a 10-minute exposure.[3] This concentration is equivalent to a teaspoon of agent released into a one-meter-high layer of air covering the area of over 100 football fields. If personnel cannot reliably detect VX contamination at these low concentrations, then mission-critical personnel may become incapacitated, thereby hindering mission accomplishment. Alternatively, as a conservative measure, commanders may order personnel to don individual protective equipment (IPE) when the concentration of a chemical warfare agent is unknown. Although such

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equipment does protect people, it also reduces their mission effectiveness. Therefore, monitoring even trace levels of chemical warfare agents in the environment would allow personnel to remove IPE when appropriate, thereby avoiding the physiological stress of wearing full protective clothing.[4] Furthermore, since civilian populations include children and the elderly, who can be more sensitive to the effects of chemical warfare agents at lower concentrations, a need exists to improve the use of sensors in the event of a terrorist attack on civilians.

Air Force bioenvironmental engineering units currently possess Hazardous Air Pollutants on Site (HAPSITE) systems capable of detecting, identifying, and measuring chemical warfare agents at very low concentrations, enabling personnel to make assessments of the risk of exposure.[5] The HAPSITE uses gas chromatography, which requires collecting and sometimes pretreating a gas or liquid sample before injection into a separation column (fig. 1). After moving through the separation column, the target molecules reach a detector that measures their concentration. The signal generated in the detector is then transformed into a readable electric signal for display. However, weighing approximately 70 pounds, this equipment can be cumbersome to operate, requires regular (weekly) preventive maintenance and use by specially trained personnel, and is quite expensive (over $100,000 per unit).[6] Furthermore, the HAPSITE could take upwards of 30 minutes to run in order to quantify chemical warfare agents at the lowest concentrations—not optimal in a combat environment that demands rapid response. Therefore, improvements in the sensitivity of detection and quantification, speed, and accuracy remain a pressing need.

Nanotechnology offers an approach for improving detection systems. Nanosensors operate at the molecular level, where the reaction between target molecules and sensor elements is direct—almost instantaneous—and by-products of the reaction are transferred to detection units almost instantaneously. Furthermore, nanosensors do not require a separation process to isolate the target molecules. Nanoscale sensor design (fig. 2) uses a sensing element that has a specific affinity for the target molecules. This strong, specific affinity eliminates the need for extra sample preparation, pretreatment, or a separation process. Immobilization and orientation of the sensing elements are precisely engineered so that by-products of the reaction between target molecules and sensing elements transfer to the microelectrode rapidly and accurately. The entire system can be installed in a handheld or dosimeter-type device at a much lower price than for conventional chromatography analyzers. Note, however, that the sensor is chemical specific. Therefore, identification of unknown nerve

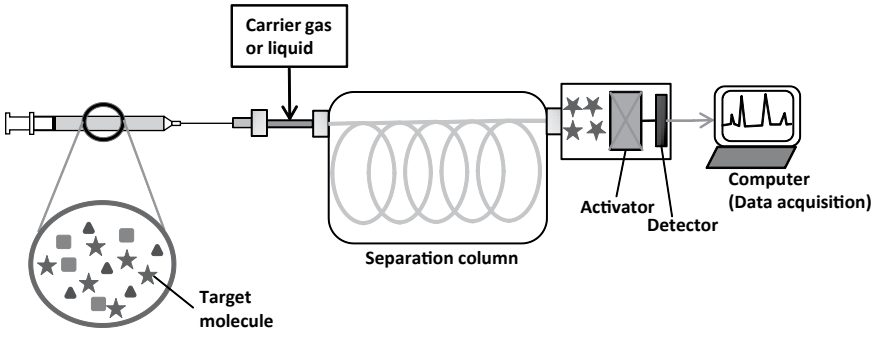

Figure 1. Schematic description of a typical gas chromatography detection system

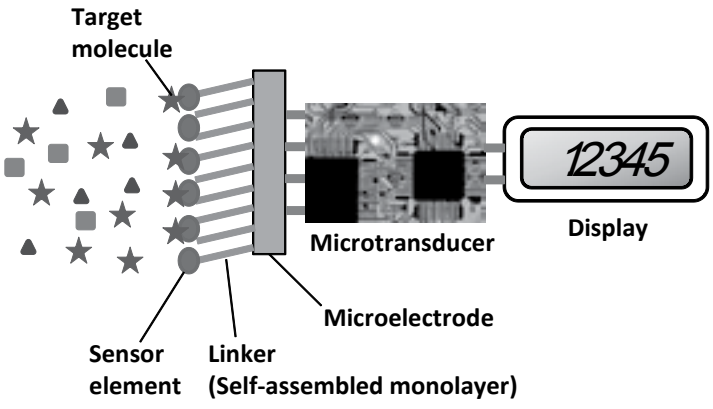

Figure 2. Schematic description of a nanosensor system on a microchip

agents will necessitate integration of several nanosensing matrices into one unit.

Researchers at UT and AFIT are developing an enzyme nanobiosensor for detecting OP compounds such as the nerve gas component dimethylmethylphosphonate (DMMP), used in the synthesis of sarin nerve agent. The sensor is classified as a biosensor because it uses an enzyme to detect the target molecule. DMMP, among the most toxic substances known and a suspected carcinogen, may prove lethal if inhaled, swallowed, or absorbed through the skin. OP compounds incapacitate and kill, primarily by inhibiting an enzyme essential for the functioning of the central nervous system in humans, thus interfering with muscle activity and producing serious symptoms and eventual death.[7]

Effective detection of DMMP involves use of the enzyme organophosphorus hydrolase (OPH) as the sensor element due to its high affinity for DMMP. Since the enzyme is an organic chemical, it may degrade and lose its effectiveness because of a phenomenon called deactivation. Therefore, the enzyme is first placed within a protective peptide nanotube (PNT). Researchers are using PNTs for this purpose because they are simple to synthesize and have high chemical and thermal stability, good conductivity, excellent biocompatibility, and functional flexibility.[8] In preliminary tests, the OPH enzyme within the PNT was four times stabler than free enzymes. An OPH can be attached readily to the inside wall of a PNT, which is then attached to a specially prepared linker called a self-assembled monolayer to form a sensor matrix on an electrode (see fig. 2). OPH-based biosensors are effective for directly monitoring and measuring various OPs ranging from OP-based pesticides and insecticides to chemical warfare agents like sarin.[9] The detection limit for the biosensor is in the range of 0.005–0.01 mg/m^3 of DMMP in air.[10] Therefore, the biosensor—two to four times more sensitive than conventional detection equipment—can detect extremely low concentrations that result in nonlethal but significant effects on humans. Moreover, the biosensor produces results three times faster than conventional detectors. In addition, the biosensor's reduced size and increased sensitivity could make it well suited for installation on a remotely piloted aircraft—a very significant military application since these aircraft are becoming increasingly important on the battlefield and for reconnaissance missions. This kind of application would allow for remote sensing of airborne chemicals, facilitating safer and more efficient sampling. Although this application exists only in the concept stage, it has great potential. Because the nanosensor under development is compound-specific, it would

respond only to the target molecule and would not likely be subject to interference from other compounds.

Along with the PNTs used to protect the OPH enzyme, research is also concentrating on the self-assembled monolayer linker, which plays an important role in the nanosensor matrix because it controls the rate of electron transfer from the OPH to the sensor. Researchers are investigating various combinations of linker molecules and sizes in order to optimize sensor performance. AFIT and UT investigators are testing the electron transfer rate and precision of the signal for different combinations of short and long linkers. On the one hand, short linkers speed up that rate (therefore, they are sensitive), but the capacitance of the short-linker layer is not low enough to suppress noise coming from other electrolytes (therefore, short linkers are not precise). On the other hand, long linkers reduce noise (therefore, they are precise), but electron transfer is slow. Consequently, optimum sensitivity and precision performance will emerge from a proper combination of the short- and long-linker molecules.

As stated above, two critical problems—enzyme deactivation and reduced sensitivity/precision—arise in enzyme sensors. The UT and AFIT researchers are addressing these problems by (1) using PNTs to protect the enzyme and increase service life, and (2) specially designing linker molecules to maximize both sensitivity and precision.

Nanotechnology has great potential for making handheld, fast, and accurate OP sensors. Fabrication of a small yet very sensitive and accurate sensor for installation on a remotely piloted aircraft could have significant military value. Similarly, handheld sensors have notable, worthwhile applications for combat and homeland defense. Fast, accurate, and inexpensive detectors could be deployed to give population centers and military installations early warning of a chemical strike. Following an attack, a reconnaissance team may need to sample several base sites before determining the proper protection requirement for personnel. Even if biosensors reduce the amount of sampling time typical of conventional methods by just a few minutes, the cumulative time savings could be substantial. Furthermore, improved detection sensitivity would inspire more confidence during the determination of risk in areas with low concentrations of chemical contamination. If personnel can safely reduce the time spent wearing IPE following an attack, then mission effectiveness would increase. Similarly, if nonlethal but mission-impairing concentrations of OP agents exist, commanders could direct personnel to don IPE. This biosensor technology offers a more cost-effective and improved chemical detection method for meeting current and future threats. Additionally, PNT is a novel material that enhances OPH enzyme activity and shelf life essential to nanoscale biosensors. Clearly, the Air Force would do well to support development and commercialization of such devices. ✪

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Notes

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